

CLAIMS

1. A method of inhibiting thrombin-induced platelet or other cell activation comprising administering to an individual in need of such treatment an effective amount of a compound comprising one or more segments having the amino acid sequence  $X_1$ -Arg-Pro-Pro- $X_2$ , wherein the compound has a formula selected from the group consisting of:

$X_1$ -Arg-Pro-Pro- $X_2$ ; and

$L-(X_1\text{-Arg-Pro-Pro-}X_2)_n$ ;

wherein:

$X_1$ , which may be the same or different in each segment, is from zero to thirty natural or synthetic amino acids;

$X_2$ , which may be the same or different in each segment, is from zero to thirty natural or synthetic amino acids, provided that the N-terminal amino acid of  $X_2$  is not glycine;

$L$  is a linker comprising a covalent bond or chemical group; and  
 $n$  is an integer from two to twenty.

2. The method of claim 1 wherein  $X_1$  is zero to seven amino acids and  $X_2$  is zero to nine amino acids.

3. The method of claim 1 wherein  $X_1$  is from zero to thirty amino acids from amino acids 1-30 of SEQ ID NO:1.

4. The method of claim 2 wherein  $X_1$  is from zero to seven amino acids from amino acids 24-30 of SEQ ID NO:1.

5. The method of claim 1 wherein the compound comprises two or more segments and at least two of the segments are different.

6. The method of claim 1 wherein the compound comprises two or more segments and all the segments are identical.

7. The method of claim 1 wherein  $n$  is an integer from two to four.

8. The method of claim 1 wherein the compound has the formula  $L-(\text{Arg-Pro-Pro-}X_2)_n$ .

9. The method of claim 8 wherein the compound has the formula

42

- 40 -

L-(Arg-Pro-Pro)<sub>n</sub>.

10. The method of claim 1 wherein the compound is selected from the group consisting of:

- (a) Arg-Pro-Pro;
- (b) Arg-Pro-Pro-Ala-Phe (SEQ ID NO:6);
- (c) Arg-Pro-Pro-Lys  
Arg-Pro-Pro-Asp; and
- (d)

Arg-Pro-Pro

Arg-Pro-Pro

Arg-Pro-Pro

Arg-Pro-Pro

Lys

Lys- $\beta$ Ala.

11. A method for inhibiting ADP-induced platelet activation in vivo comprising administering to an individual in need of such treatment an effective amount of a compound comprising one or more segments having the amino acid sequence X<sub>1</sub>-Arg-Pro-Pro-X<sub>2</sub>, wherein the compound has a formula selected from the group consisting of:

X<sub>1</sub>-Arg-Pro-Pro-X<sub>2</sub>; and

L-(X<sub>1</sub>-Arg-Pro-Pro-X<sub>2</sub>)<sub>n</sub>;

wherein:

X<sub>1</sub>, which may be the same or different in each segment, is from zero to thirty natural or synthetic amino acids;

X<sub>2</sub>, which may be the same or different in each segment, is from zero to thirty natural or synthetic amino acids, provided that the N-terminal amino acid of X<sub>2</sub> is not glycine;

L is a linker comprising a covalent bond or chemical group; and n is an integer from two to twenty.

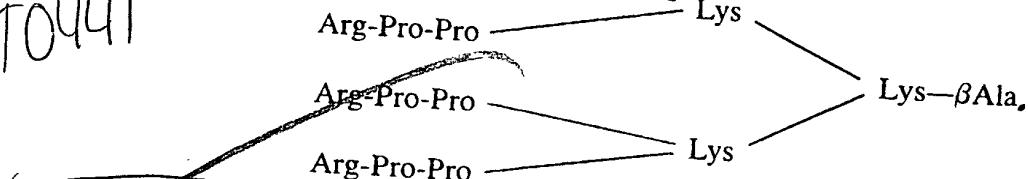
12. The method of claim 11 wherein X<sub>1</sub> is zero to seven amino acids and X<sub>2</sub> is zero to nine amino acids.

43

- 41 -

13. The method of claim 12 wherein the compound is selected from the group consisting of:

- (a) Arg-Pro-Pro;
- (b) Arg-Pro-Pro-Ala-Phe (SEQ ID NO:6);
- (c) Arg-Pro-Pro-Lys  
Arg-Pro-Pro-Asp; and
- (d)



14. A method for preventing platelet aggregation comprising administering to an individual in need of such treatment an effective amount of a compound comprising one or more segments having the amino acid sequence  $X_1$ -Arg-Pro-Pro- $X_2$ , wherein the compound has a formula selected from the group consisting of:

$$X_1\text{-Arg-Pro-Pro-}X_2; \text{ and}$$

$$L\text{-}(X_1\text{-Arg-Pro-Pro-}X_2)_n;$$

wherein:

$X_1$ , which may be the same or different in each segment, is from zero to thirty natural or synthetic amino acids;

$X_2$ , which may be the same or different in each segment, is from zero to thirty natural or synthetic amino acids, provided that the N-terminal amino acid of  $X_2$  is not glycine;

$L$  is a linker comprising a covalent bond or chemical group; and  $n$  is an integer from two to twenty.

15. The method of claim 14 wherein  $X_1$  is zero to seven amino acids and  $X_2$  is zero to nine amino acids.

44

- 42 -

16. The method of claim 14 wherein  $X_1$  is from zero to thirty amino acids from amino acids 1-30 of SEQ ID NO:1.

17. The method of claim 15 wherein  $X_1$  is from zero to seven amino acids from amino acids 24-30 of SEQ ID NO:1.

18. The method of claim 14 wherein the compound comprises two or more segments and at least two of the segments are different.

19. The method of claim 14 wherein the compound comprises two or more segments and all the segments are identical.

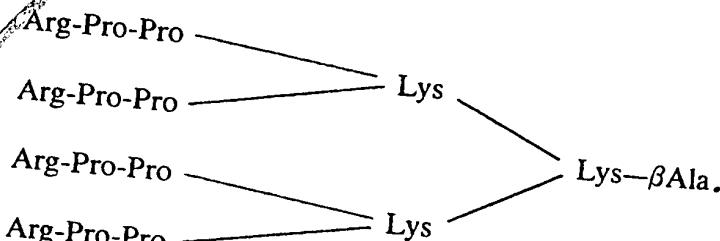
20. The method of claim 14 wherein  $n$  is an integer from two to four.

21. The method of claim 14 wherein the compound has the formula  $L-(\text{Arg-Pro-Pro-}X_2)_n$ .

22. The method of claim 21 wherein the compound has the formula  $L-(\text{Arg-Pro-Pro})_n$ .

23. The method of claim 14 wherein the compound is selected from the group consisting of:

- (a) Arg-Pro-Pro;
- (b) Arg-Pro-Pro-Ala-Phe (SEQ ID NO:6);
- (c) Arg-Pro-Pro-Lys  
|  
Arg-Pro-Pro-Asp; and
- (d)

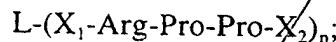


24. A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a compound comprising one or more segments having the amino acid sequence  $X_1\text{-Arg-Pro-Pro-}X_2$ , wherein the compound has a formula selected from the group consisting of:

$X_1\text{-Arg-Pro-Pro-}X_2$ ; and

4/S

- 43 -



wherein:

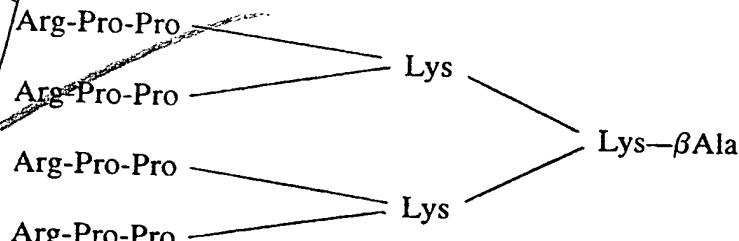
$X_1$ , which may be the same or different in each segment, is from zero to thirty natural or synthetic amino acids;

$X_2$ , which may be the same or different in each segment, is from zero to thirty natural or synthetic amino acids, provided that the N-terminal amino acid of  $X_2$  is not glycine;

L is a linker comprising a covalent bond or chemical group; and  
n is an integer from two to twenty.

25. The pharmaceutical composition of claim 24 comprising a pharmaceutically acceptable carrier and a compound having a formula selected from the group consisting of:

- (a) Arg-Pro-Pro;
- (b) Arg-Pro-Pro-Ala-Phe (SEQ ID NO:6);
- (c) Arg-Pro-Pro-Lys  
  - Arg-Pro-Pro-Asp; and ]
- (d)



26. A method for identifying compounds that selectively inhibit thrombin-induced platelet and other cell activation comprising measuring the ability of the compounds to bind to the thrombin cleavage site on the thrombin receptor.

27. The method of claim 26 wherein the compounds are present in a combinatorial library.

460

- 44 -

26. The method of claim 26 further comprising:

- (a) measuring the ability of the compounds to inhibit thrombin-induced platelet aggregation; and
- (b) measuring the ability of the compounds to inhibit thrombin-induced calcium mobilization in fibroblasts.

5

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